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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/042,421	SACKSTEIN, ROBERT	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/08/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/08/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114.

Applicant's submission, filed on 06/08/2009, has been entered.

Applicant's amendment, filed 06/08/2009, has been entered.

Claim 1 has been amended.

Claims 5-6 and 8-65 have been canceled.

Claims 1-4 and 7-8 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's amendment, filed 06/08/2009.

The rejections of record can be found in the previous Office Action.

3. Priority:

As indicated previously,

Upon a review of USSN 60/240,987, the priority application USSN 60/240,987 does not support the broader claims of the instant application.

USSN 60/240,987 appears directed to the distinct glycoform of CD44 as an L-selectin ligand on human hemopoietic progenitor cells, namely HCLL-CD44, that is a 98 kD KG1a CD44 membrane protein and which may have 120 / 130 kD bands that reflect isoforms that were designated CD44R2 and CD44Ra, respectively (see entire document, including Results). This provisional application was directed to identifying an unknown/ unassigned adhesion molecule, which was shown to have a previously unrecognized function of a well-characterized adhesion molecule (e.g. see pages 4-5, overlapping paragraph of USSN 60/240,987).

The instant claims are broader in scope than the particular adhesion molecule HCLL-CD44 identified and characterized in the priority document.

Further, it does not appear that priority USSN 60/240,987 provides sufficient written description for the claims nucleotide sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene, wherein the CD44 polypeptide is a human CD44H, human CD44R1 or human CD44R2", "CD44 polypeptide comprises HECA-452 reactive sialyated, fucosylated N-glycans", wherein said glycosylated CD44 polypeptide is a ligand for both an E-selectin and L-selectin", and "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide", as currently recited and as more broadly recited than previously described in USSN 60/240,987.

Also, it is noted that it does not appear that the priority USSN 60/240,987 provides sufficient written description for the limitations of the dependent claims, again as currently recited and more broadly recited than previously described in USSN 60/240,987.

Again, if applicant desires priority back to USSN 60/240,987, filed 10/18/2000;
applicant has been invited to point out and provide documentary support for the priority of the instant claims.

Applicant has been reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

A claim as a whole has only one effective filing date.
See e.g. Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

Applicant has been reminded that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed.
See Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Therefore, the effective filing date of the instant claims has been deemed to be the filing date of the provisional USSN 60/297,474, filed 06/11/2001.

Applicant's amendment, filed 01/31/2008, doid not dispute the effective priority of the instant claims.

4. Upon reconsideration of applicant's arguments, filed 06/08/2009, the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Sackstein et al. (Blood 89: 2773 – 2781, 1997), as further evidenced by Dimitroff et al. (J. Biol. Chem. 276: 47623 – 47631, 2001) and Sackstein (J. Invest. Dermatol. 122: 1061-1069, 2004) has been withdrawn in view of the recitation of "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

5. Upon reconsideration of applicant's arguments, filed 06/08/2009, the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Stamenkovic et al. (EMBO Journal 10: 343 –348, 1991) (see entire document, including Figure 1) as evidenced by Sackstein (US 2003/0040607 A1) and Sackstein (J. Invest. Dermatol. 122: 1061-1069, 2004) has been withdrawn in view of the recitation of "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

6. Upon reconsideration of applicant's arguments, filed 06/08/2009, the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ) (see entire document) as further evidenced by Dimitroff et al. (J. Biol. Chem. 276: 47623 – 47631, 2001) and Sackstein (J. Invest. Dermatol. 122: 1061-1069, 2004) has been withdrawn in view of the recitation of "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

7. For clarity including applicant's arguments that the primary references cannot be applied to all of the claims equally,

the rejection under 35 U.S.C. § 103(a) has been separated into a rejection under 35 U.S.C. § 103(a) as being unpatentable on each primary reference over Sackstein et al. (Blood 89: 2773 – 2781, 1997) (of record) OR Stamenkovic et al. (EMBO Journal 10: 343 –348, 1991) (of record) OR Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ).

Also, New Grounds of Rejection have been set forth herein.

With respect to applicant's arguments in conjunction with various references as well as the Picker Declaration under 37 CFR 1.132, the following is noted.

In contrast to applicant's arguments in conjunction with various references as well as the Picker Declaration under 37 CFR 1.132,, Sackstein et al., Stamenkovic et al. and Dougherty et al. each on their own teach the identification of a CD44H, CD44R1, HCELL molecule, including a suficient expectation of success of the existence and isolation of said molecule expressed on the KG1a or Namalwa cell line which mediates attachment of cells to endothelial cells (e.g., see above) that would encompass the structural and functional characteristics encompassed by the claimed invention and wherein the ordinary artisan would have isolated to a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The prior art provides for the key starting materials (e.g., KG1a, Namalwa), probes to isolate CD44H, CD44R1 and HCELL (e.g., L-selectin ligand probes or CD44 probes) as well as functional and structural characteristics for said molecules (see above) to isolate said molecules having the structural and functional characteristics (e.g., encompassed by the claimed by well known techniques known and practiced by the ordinary artisan at the time the invention was made invention and wherein reference molecule reading on the claimed invention would have been purified and provided in a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

Given the starting materials, known probes and structural/functional characteristics associated with the referenced CD44H, CD44R1 and/or HCELL molecules, the ordinary artisan would have isolated said molecules with those structural and functional characteristics observed in KG1a or Namalwa cell lines (versus COS cells).

Applicant's arguments concerning distinguishing the particular CD44 glycoform encompassed by the claimed invention, including the reliance upon Maiti et al., Kathoh et al., Picker, Berg, Jutila and Walcheck references as well as the Picker Declaration under 37 CFR 1.132,, appear to ignore the relationship of the referenced molecules to a human hemopoietic stem cell line or a Burkitt lymphoma cell line.

The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144.

That the prior art did not isolate the referenced CD44H, CD44R1 or HCELL to the extent currently recited or that the prior art did not teach all of the claimed recitations,

the ordinary artisan would have a reasonable expectation of success of isolating said referenced molecules from either KG1a or Namalwa cell lines to a level of purity recited in the instant claims, wherein said molecules would have been expected to retain the structural and functional characteristics of these molecules as they existed on the KG1a or Namalwa cell lines. The claimed functional and structural characteristics of the claimed CD44H would have been met by the isolated of these molecules as they existed on the KG1a or Namalwa cell lines, whether the ordinary artisan knew of each characteristic of these molecules or not.

While no single reference teaches a CD44 glycoform having E-selectin or L-selectin activity per se,

each reference does provide an identification of a particular molecule, which is expressed on a particular cell type or cell line, wherein said molecule has certain structural and functional characteristics, including involving cell adhesion, and, in turn, can be distinguished from other cell adhesion molecules.

In consideration of the discrepancies often encountered in the art between protein molecular weight when determined by different methods, when a molecular weight is recited to characterize a protein the claims should include not only the method by which it was determined, e.g. whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, but also whether the determination was made under denaturing or non-denaturing conditions and whether reducing or non-reducing conditions were are used.

The rationale to support a conclusion that the claims would have been obvious is that all the claimed elements (e.g, identification of molecule of interest by distinguishing structure/function and source cell line) were known in the prior art and one skilled in the art could have arrived at the claimed invention by using known methods (isolating and purifying molecules of interest) with no change in their respective functions and the combination would have yielded nothing more than predictable results of isolating a molecule that reads on the claimed glycosylated CD44H polypeptide, including "wherein a preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The rationale to support a conclusion that the claims would have been obvious is that a preparing a glycosylated CD44H polypeptide in "a preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide" was made part of ordinary capabilities of one skilled in the art based upon the teachings of the prior art. One of ordinary skill in the art would have been capable of applying the known recombinant methods of isolating and purifying glycosylated proteins or interest and preparing compositions of said purified/isolated forms of glycosylated proteins of interest for a variety of utilities, wheih would have been predictable to one of ordinary skill in the art at the time the invention was made.

The rationale to support a conclusion that the claims would have been obvious is that a particular known technique (isolating and purifying glycosylated proteins of interest and preparing compositions comprising said isolated/purified proteins) was recognized as part of the ordinary capabilities of one skilled in the art. One of ordinary skill in the art would have been capable of applying these known techniques to a known product (e.g. the CD44H, CD44R1, HCELL proteins expressed on the KG1a and Namalwa cell lines) that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (isolating and purifying glycosylated proteins of interest and preparing compositions comprising said isolated/purified proteins) within his or her technical grasp. This leads to the anticipated success of (isolating and purifying glycosylated proteins of interest and preparing compositions comprising said isolated/purified proteins. It is likely the product not of innovation but of ordinary skill and common sense.

Since isolating and purifying glycosylated proteins of interest and preparing compositions comprising said isolated/purified proteins would have been predictable at the time of the invention, there would have been reasonable expectation of successful development of Isolating and purifying the CD44H, CD44R1, HCELL proteins expressed on the KG1a and Namalwa cell lines. The prior art had recognized the role of these molecules in cell adhesion and their distinguishing characteristics from other known adhesion molecules at the time the invention was made and had suggested and relied upon the isolation and purification of these molecules for various utilities associated with adhesion molecules in order to accomplish this goal. The claims were obvious because it would have been obvious to try isolating and purifying glycosylated proteins of interest and preparing compositions comprising said isolated/purified glycoproteins which would retain the structural and functional characteristics expressed on KG1a and Namalwa cells with a reasonable expectation of success.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to isolate, examine and utilize adhesion molecules such as CD44H, CD44R1 or HCELL,

incorporating known techniques to isolate and purify said glycosylated proteins of interest and preparing compositions comprising said isolated/purified glycoproteins which would retain the structural and functional characteristics expressed on KG1a and Namalwa cells would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing compositions comprising said adhesion molecules of interest.

8. Claims 1-4 and 7-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sackstein et al. (Blood 89: 2773 – 2781, 1997) (of record)

in view of art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made,

as taught by Ni et al. (U.S. Patent No. 5,942,417) (892; of record),

as taught by McEver et al. (U.S. Patent No. 6,124,267)

and as acknowledged on pages 19-24 of the instant specification and as evidenced by the following statements in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired for the reasons of record

and newly added Lasky et al. (U.S. Patent No. 5,652,343), Oxley et al. (Blood 84: 3299-3306, 1994) (1449; #AU) .

Applicant's arguments, filed 06/08/2009, have been fully considered but have not been found convincing for the reason of record reiterated herein as well as for the reasons addressed above and the newly added references herein.

With respect to Sackstein 1997, the following is noted.

While applicant focuses on the lack of Sackstein's (1997) lack of teaching of a CD44 glycoform comprising sialyated fucosylated glycans,

Sackstein 1997 clearly provides teach the identification of a glycoprotein L-selectin ligand expressed on the human hemopoietic cell line KG1a, wherein the L-selectin ligand does not contain MECA79 antibody-specific epitopes and is not dependent on sulfation.

Newly added Lasky et al. tech methods for isolating L-selectin ligands of interest (see entire document, including glycoprotein ligands and the use of L-selectin IgG for said isolation as well as their purification (E.g., see column 27, Purification of the Selectin Ligands and Examples) (e.g., see entire document, including Summary of the Invention and Detailed Description of the Invention).

Oxley et al. provides for the expression of a functional L-selectin ligand expression on the human hemopoietic stem cell lines KG1a, wherein these cells substituted for lymph node sections in functional assays, and wherein the adherence was calcium-dependent and inhibited by anti-L-selectin antibodies and by carbohydrates known to bind L-selectin, which was distinguishable from other L-selectin ligands (see entire document, including Abstract, Introduction, Materials and Methods, Results and Discussion).

This teaching of Oxley et al. provides the basis for the Sackstein et al. observations.

The teachings of the prior art, including newly added references Lasky et al. and Oxley et al. provide for a sufficient expectation of success of the existence and isolation of a L-selectin ligand to the extent that the KG1a L-selectin ligand would have the structural and functional characteristics encompassed by the claimed invention and wherein the KG1a L-selectin ligand would have isolated to a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The prior art provides for the key starting materials (e.g., KG1a cell line), probes to isolate L-selectin ligands (e.g., L-selectin IgG) as well as functional and structural characteristics for a KG1a L-selectin ligand (e.g., the teachings of Sackstein et al. and Oxley et al.) to isolate a KG1a L-selectin ligand having the structural and functional characteristics encompassed by the claimed by well known techniques known and practiced by the ordinary artisan at the time the invention was made invention and wherein the KG1a L-selectin ligand would have been purified and provided in a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The following of record is reiterated for applicant's convenience.

Applicant is reminded that the claims are drawn to "a purified preparation of a glycosylated CD44 glycosyted polypeptide.

Again, the prior art reference clearly teach the isolation of the claimed hemopoietic L-selectin ligand from KG1a cells.

Applicant's arguments and the examiner's rebuttal with respect to the teachings of Sackstein et al. (Blood 89: 2773 – 2781, 1997) have been addressed above.

Applicant's arguments appear to ignore the clear teachings in the prior art, including the inventor's own prior art reference Sackstein et al. (Blood 89: 2773 – 2781, 1997), that the hemopoietic L-selectin ligand expressed on KG1a cells were known in the prior art.

For example, note the following from page 1064, column 1 of Sackstein et al. (J. Invest. Dermatol. 122: 1061-1069, 2004) (892; of record)

As stated above, the bone marrow microvasculature is like that of skin in that it displays constitutive expression of E- and P-selectin (Schweitzer et al, 1996; Frenette et al, 1998). There is increasing evidence these molecules play important roles in trafficking of primitive hematopoietic cells into bone marrow (Frenette et al, 1998; Mazo et al, 1998; Hidalgo et al, 2002; Katayama et al, 2003). Although the identity of the true HSC is debated, for the purposes of this review we will consider CD34+ cells lacking lineage-specific markers (i.e., CD34+/lineage- cells) as the representative population of HSC. Human HSC express PSGL-1 and another selectin ligand, HCELL (Oxley and Sackstein, 1994; Sackstein et al, 1997; Dimitroff et al, 2000, 2001a; Sackstein and Dimitroff, 2000). HCELL was initially identified operationally as an L-selectin ligand, and was distinguished from all other L-selectin ligands by a number of biochemical features: (1) Sulfation-independent binding activity; (2) functional resistance to O-sialoglycoprotease digestion; (3) absence of MECA79 antigens; and (4) L-selectin binding determinants that were expressed on N-glycans rather than O-glycans (Oxley and Sackstein, 1994; Sackstein et al, 1997; Sackstein and Dimitroff, 2000). Although initially considered to be a "novel" selectin ligand by the above biochemical criteria, mass spectrometry subsequently revealed that HCELL is not novel per se: it is a glycoform of a well-recognized integral membrane glycoprotein, CD44, that expresses the CLA epitope (i.e., is recognized by mAb HECA452). In contrast to PSGL-1 that displays CLA on O-glycans, however, the CLA determinant(s) and the E-/L-selectin binding sites of HCELL are on N-glycans.

Again it is maintained that given the teachings of isolating and characterizing the structure of the claimed hemopoietic L-selectin ligand expressed on KG1a cells.
one of ordinary skill would have immediately envisaged or readily have expected the isolation of HCELL / KG1a glycosylated proteins including "isolated or purified protein that is substantially free of cellular materials or other contaminating protein from the cell or tissue source form which HCELL glycoprotein is derived or substantially freed form chemical precursors or other chemical when chemically synthesized , including being recombinantly produced, which is also free of culture medium (e.g. see page 11, paragraph 3 of the instant specification), thereby meeting the claimed limitation of "wherein the preparation comprises less that 5% of a polypeptide other than the glycosylated CD44 polypeptide" at the time the invention

In turn, one of ordinary skill in the art would have immediately envisaged or readily employed isolated HCELL / KG1a L-selectin ligand in the form of "a sterile aqueous solution", as currently claimed;
given the routine use of such "sterile aqueous solutions" to manipulate isolated proteins of use at the time the invention was made by the ordinary artisan.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

Also, given the use of adhesion molecule- / selectin-related proteins of interest for various diagnostic/therapeutic utilities as taught by McEver et al. (e.g., see columns 11-15) and by Ni et al. (e.g., see columns 28-37),
it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide adhesion molecules of interest

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to isolate, characterize and employ CD44 proteins of interest at the time the invention was made,
incorporating of the KG1a L-selectin ligand / HCELL into purified preparations, including forms of sterile aqueous solutions, dispersions and powders would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing purified preparations of glycosylated adhesion glycoproteins of interest.

The following of record is reiterated for applicant's convenience.

Again, it is noted that Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ) as well as McEver et al. (U.S. Patent No. 6,124,267) as well as applicant's acknowledgement in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.

Sackstein et al. differ from the claimed invention by not disclosing the purity of their referenced KG1a L-selectin ligand or that they do not exemplify the isolation of their referenced KG1a L-selectin ligand via known and practiced recombinant methods to isolate and express proteins of interest by the ordinary artisan at the time the invention was made.

Ni et al. teach the known and practiced methods of isolating and expressing isolated proteins of interest, including its application to glycosylated proteins of interest at the time the invention was made (see entire document, including Summary of the Invention, Detailed Description and Examples). Also, note that Ni et al. teach that isolated encompasses removed from its native environment, purified and produced by recombinant means (e.g. see column 18, paragraph 1).

McEver et al. teach the known manipulation and expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made (see entire document, including Detailed Description of the Invention, including Expression Systems on columns 9-11 and Examples on columns 15-44).

Consistent with the prior art of record and newly added McEver et al.,
Pages 19-24 of the instant specification acknowledges the art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made.
For example, page 20, paragraph 2 of the instant specification states that
It would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.
In this Section on HCELL Recombinant Expression Vectors and Host Cells,
It is noted that applicant also relies upon prokaryotic and eukaryotic cells, including CHO or COS cells, as well as tissue-specific regulatory elements known and practiced at the time the invention was made.

Given the teachings of Sackstein et al. concerning the expression and role of the HCELL as it reads on the claimed CD44 glycoform, one of ordinary skill in the art would have isolated and produced glycoforms via various known means at the time the invention was made, including recombinant means as a standard practice to investigate the role and use of said adhesion molecule glycoforms with the structural and functional properties described by Sackstein et ein. in physiological events. Given the standard practices of isolating and recombinantly expressing antigens, including adhesion molecules such as HCELL glycoforms as well as the known manipulation and

expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made, one of ordinary skill in the art had a reasonable expectation of success in preparing the HCELL as it reads on the claimed CD44 glycoform in preparation comprising less than 5% of HCELL as it reads on the CD44 glycoform. The advantages of isolated and purified molecules of interest, including adhesion molecules such as HCELL as it reads on the claimed CD44 glycoforms, were well known and practiced in the art at the time the invention was made in order to study and characterize the molecule / protein of interest for structure-function relationships as well as to employ such proteins for a wide variety of utilities associated with the molecule / protein of interest. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

9. Claims 1-4 and 7-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Stamenkovic et al. (EMBO Journal 10: 343 –348, 1991) (of record)
in view of art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made,
as taught by Ni et al. (U.S. Patent No. 5,942,417) (892; of record),
as taught by McEver et al. (U.S. Patent No. 6,124,267)
and as acknowledged on pages 19-24 of the instant specification and as evidenced by the following statements in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired for the reasons of record.

Applicant's arguments, filed 06/08/2009, have been fully considered but have not been found convincing for the reason of record reiterated herein as well as for the reasons addressed above.

Applicant does not address the issue that Stamenkovic et al. teach the hemopoietic form of CD44 (i.e., CD44H) was expressed on the Burkitt lymphoma cell line Namalwa (e.g., see Results on pages 344-345 and Materials and Methods on pages 347-348).

Applicant has not provided sufficient objective evidence concerning the absence of the expression of the CD44H encompassed by the claimed invention on the Burkitt lymphoma cell line Namalwa.

The teachings of the prior art provide for a sufficient expectation of success of the existence and isolation of a CD44H that bestowed binding competence for lymph node high endothelail cells (e.g., see Abstract, Introduction, Results and Discussion) that would encompass the structural and functional characteristics encompassed by the claimed invention and wherein the ordinary artisan would have isolated to a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The prior art provides for the key starting materials (e.g., Burkitt lymphoma cell line Namalwa), probes to isolate L-selectin ligands (e.g., anti-CD44 antibodies) as well as functional (CD44H bestowed binding competence for lymph node high endothelial cells) and structural characteristics for a CD44H (e.g., the teachings of Stamenkovic) to isolate a CD44H having the structural and functional characteristics (E.g., encompassed by the claimed by well known techniques known and practiced by the ordinary artisan at the time the invention was made invention and wherein the CD44H would have been purified and provided in a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

Also, with respect to applicant's arguments; in consideration of the discrepancies often encountered in the art between protein molecular weight when determined by different methods, when a molecular weight is recited to characterize a protein the claims should include not only the method by which it was determined, e.g. whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, but also whether the determination was made under denaturing or non-denaturing conditions and whether reducing or non-reducing conditions were are used.

The following is reiterated for applicant's convenience.

Applicant is reminded that the claims are drawn to "a purified preparation of a glycosylated CD44 polypeptide / CD44H".

Again, the prior art references clearly teach the isolation of the claimed hemopoietic CD44H, including their expression on various hemopoietic cells and cell lines, including the Namalwa cell lines.

Applicant's arguments and the examiner's rebuttal with respect to the teachings of Stamenkovic et al. (EMBO Journal 10: 343 –348, 1991) have been addressed above.

Again it is maintained that given the teachings of isolating and characterizing the structure of the claimed hemopoietic CD44H, including their expression on various hemopoietic cells and cell lines, including the Namalwa cell line.

one of ordinary skill would have immediately envisaged or readily have expected the isolation of CD44H glycosylated proteins including "isolated or purified protein that is substantially free of cellular materials or other contaminating protein from the cell or tissue source form which CDH glycoprotein is derived or substantially freed form chemical precursors or other chemical when chemically synthesized , including being recombinantly produced, which is also free of culture medium (e.g. see page 11, paragraph 3 of the instant specification), thereby meeting the claimed limitation of "wherein the preparation comprises less that 5% of a polypeptide other than the glycosylated CD44 polypeptide" at the time the invention

In turn, one of ordinary skill in the art would have immediately envisaged or readily employed isolated CD44H / Namalwa CD44 protein in the form of "a sterile aqueous solution", as currently claimed;

given the routine use of such "sterile aqueous solutions" to manipulate isolated proteins of use at the time the invention was made by the ordinary artisan.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

Also, given the use of adhesion molecule- / selectin-related proteins of interest for various diagnostic/therapeutic utilities as taught by McEver et al. (e.g., see columns 11-15) and by Ni et al. (e.g., see columns 28-37),

it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide CD44 polypeptides of interest

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to isolate, characterize and employ CD44 proteins of interest at the time the invention was made,

incorporating of CD44H / Namalwa CD44 glycosylated proteins into purified preparations, including forms of sterile aqueous solutions, dispersions and powders would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing purified preparations of glycosylated CD44 polypeptides of interest.

The following of record is reiterated for applicant's convenience.

Again, it is noted that Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ) as well as McEver et al. (U.S. Patent No. 6,124,267) as well as applicant's acknowledgement in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.

Stamenkovic et al. differ from the claimed invention by not disclosing the purity of their referenced CD44 glycoforms or that they do not exemplify the isolation of their referenced CD44 glycoforms via known and practiced recombinant methods to isolate and express proteins of interest by the ordinary artisan at the time the invention was made.

Ni et al. teach the known and practiced methods of isolating and expressing isolated proteins of interest, including its application to CD44 proteins at the time the invention was made (see entire document, including Summary of the Invention, Detailed Description and Examples). Also, note that Ni et al. teach that isolated encompasses removed from its native environment, purified and produced by recombinant means (e.g. see column 18, paragraph 1).

McEver et al. teach the known manipulation and expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made (see entire document, including Detailed Description of the Invention, including Expression Systems on columns 9-11 and Examples on columns 15-44).

Consistent with the prior art of record and newly added McEver et al.,
Pages 19-24 of the instant specification acknowledges the art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made.
For example, page 20, paragraph 2 of the instant specification states that
It would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.
In this Section on HCELL Recombinant Expression Vectors and Host Cells,
It is noted that applicant also relies upon prokaryotic and eukaryotic cells, including CHO or COS cells, as well as tissue-specific regulatory elements known and practiced at the time the invention was made.

Given the teachings of Stamenkovic et al. concerning the expression and role of the claimed CD44 glycoforms, one of ordinary skill in the art would have isolated and produced CD44 glycoforms via various known means at the time the invention was made, including recombinant means as a standard practice to investigate the role and use of said CD44 glycoforms in physiological events. Given the standard practices of isolating and recombinantly expressing antigens, including adhesion molecules such as CD44 glycoforms as well as the known manipulation and expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made, one of ordinary skill in the art had a reasonable expectation of success in preparing the claimed CD44 glycoform in preparation comprising less than 5% of the CD44 glycoform other than the glycosylated CD44 polypeptide. The advantages of isolated and purified molecules of interest, including adhesion molecules as CD44 glycoforms, were well known and practiced in the art at the time the invention was made in order to study and characterize the molecule / protein of interest for structure-function relationships as well as to employ such proteins for a wide variety of utilities associated with the molecule / protein of interest. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

10. Claims 1-4 and 7-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ)
in view of art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made,
as taught by Ni et al. (U.S. Patent No. 5,942,417) (892; of record),
as taught by McEver et al. (U.S. Patent No. 6,124,267)
and as acknowledged on pages 19-24 of the instant specification and as evidenced by the following statements in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired for the reasons of record.

Applicant's arguments, filed 06/08/2009, have been fully considered but have not been found convincing for the reason of record reiterated herein as well as for the reasons addressed above and the newly added references herein.

The teachings of the prior art provide for a sufficient expectation of success of the existence and isolation of a CD44 expressed on the KG1a cell line which mediates attachment of cells to endothelial cells (e.g., see Introduction and Discussion) that would encompass the structural and functional characteristics encompassed by the claimed invention and wherein the ordinary artisan would have isolated to a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The prior art provides for the key starting materials (e.g., KG1a), probes to isolate CD44 glycoforms (e.g., anti-CD44 antibodies) as well as functional (CD44 mediated attachment of cells to endothelial cells) and structural characteristics for a KG1a CD44 to isolate a KG1a CD44 having the structural and functional characteristics (e.g., encompassed by the claimed by well known techniques known and practiced by the ordinary artisan at the time the invention was made invention and wherein the KG1a CD44 would have been purified and provided in a composition "wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide / glycosylated polypeptide".

The following is reiterated for applicant's convenience.

Applicant is reminded that the claims are drawn to "a purified preparation of a glycosylated CD44H polypeptide.

Again, the prior art references clearly teach the isolation of the claimed hemopoietic CD44H via the KG1a CD44.

Again it is maintained that given the teachings of isolating and characterizing the structure of the claimed hemopoietic CD44H, including their expression on various hemopoietic cells and cell lines, including the KG1a cell lines.
one of ordinary skill would have immediately envisaged or readily have expected the isolation of KG1a CD44 glycosylated proteins including "isolated or purified protein that is substantially free of cellular materials or other contaminating protein from the cell or tissue source form which HCELL glycoprotein is derived or substantially freed form chemical precursors or other chemical when chemically synthesized , including being recombinantly produced, which is also free of culture medium (e.g. see page 11, paragraph 3 of the instant specification), thereby meeting the claimed limitation of "wherein the preparation comprises less that 5% of a polypeptide other than the glycosylated CD44 polypeptide" at the time the invention

In turn, one of ordinary skill in the art would have immediately envisaged or readily employed isolated KG1a CD44 protein in the form of "a sterile aqueous solution", as currently claimed;
given the routine use of such "sterile aqueous solutions" to manipulate isolated proteins of use at the time the invention was made by the ordinary artisan.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

Also, given the use of adhesion molecule- / selectin-related proteins of interest for various diagnostic/therapeutic utilities as taught by McEver et al. (e.g., see columns 11-15) and by Ni et al. (e.g., see columns 28-37),
it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide CD44 polypeptides of interest

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to isolate, characterize and employ CD44 proteins of interest at the time the invention was made,
incorporating of KG1a CD44 glycosylated proteins into purified preparations, including forms of sterile aqueous solutions, dispersions and powders would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing purified preparations of glycosylated CD44 polypeptides of interest.

The following of record is reiterated for applicant's convenience.

Again, it is noted that Dougherty et al. (J. Exp. Med. 174: 1-5, 1991) (1449; #AJ) as well as McEver et al. (U.S. Patent No. 6,124,267) as well as applicant's acknowledgement in the instant specification that it would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.

As indicated above
Dougherty et al. teach the isolation and molecular cloning of CD44R1 and CD44R2, as well as their expression on various hemopoietic cells and cell lines, including the KG1a cell lines.
Given the teaching of the structural characterization (e.g. amino acid and encoding nucleic acids) of CD44R1 and CD44R2 isoforms as well as hemopoietic source of said CD44R1 and CD44R2 isoforms, which is consistent with the instant disclosure as well as instant claims 62-64 as well as the breadth of the instant claims, the prior art appears to read on the claimed polypeptides, in the absence of objective evidence to the contrary.
Dougherty et al. differs from the claimed invention by not being explicit in terms of certain structural or functional characteristics as currently claimed.

Dougherty et al. differ from the claimed invention by not disclosing the purity of their referenced CD44 glycoforms or that they do not exemplify the isolation of their referenced CD44 glycoforms via known and practiced recombinant methods to isolate and express proteins of interest by the ordinary artisan at the time the invention was made.

Ni et al. teach the known and practiced methods of isolating and expressing isolated proteins of interest, including its application to CD44 proteins at the time the invention was made (see entire document, including Summary of the Invention, Detailed Description and Examples). Also, note that Ni et al. teach that isolated encompasses removed from its native environment, purified and produced by recombinant means (e.g. see column 18, paragraph 1).

McEver et al. teach the known manipulation and expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made (see entire document, including Detailed Description of the Invention, including Expression Systems on columns 9-11 and Examples on columns 15-44).

Consistent with the prior art of record and newly added McEver et al.,
Pages 19-24 of the instant specification acknowledges the art known and practiced procedures to isolate and express isolated or purified proteins of interest at the time the invention was made.
For example, page 20, paragraph 2 of the instant specification states that
It would be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired.
In this Section on HCELL Recombinant Expression Vectors and Host Cells,
It is noted that applicant also relies upon prokaryotic and eukaryotic cells, including CHO or COS cells, as well as tissue-specific regulatory elements known and practiced at the time the invention was made.

Given the teachings of Dougherty concerning the expression and role of the claimed CD44 glycoforms, one of ordinary skill in the art would have isolated and produced CD44 glycoforms via various known means at the time the invention was made, including recombinant means as a standard practice to investigate the role and use of said CD44 glycoforms in physiological events. Given the standard practices of isolating and recombinantly expressing antigens, including adhesion molecules such as CD44 glycoforms as well as the known manipulation and expression of proteins of interest that are associated with sialylated and fucosylated glycans and that interact with selectins, including the use of fucosyltransferases in the expression and anyalysis of said proteins of interest at the time the invention was made, one of ordinary skill in the art had a reasonable expectation of success in preparing the claimed CD44 glycoform in preparation comprising less than 5% of the CD44 glycoform other than the glycosylated CD44 polypeptide. The advantages of isolated and purified molecules of interest, including adhesion molecules as CD44 glycoforms, were well known and practiced in the art at the time the invention was made in order to study and characterize the molecule / protein of interest for structure-function relationships as well as to employ such proteins for a wide variety of utilities associated with the molecule / protein of interest. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

11. Given the abandonment of USSN 11/032,256, the previous rejection under the judicially created doctrine of obviousness-type double patenting has been withdrawn.

12. It is noted that applicant has a number of copending applications drawn to CD44 glycosylated isoforms, particularly to those associated with HCELL.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

13. No claim allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/
Primary Examiner
Technology Center 1600
Art Unit 1644
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